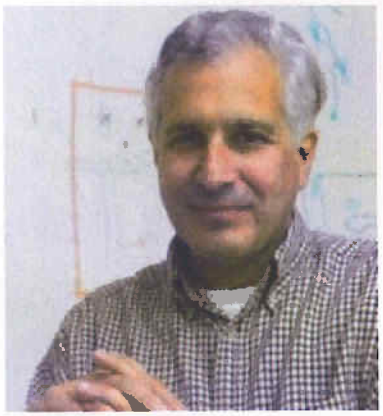
know what to relate them to. So that's typically why it's desirable to overlay that with the electron microscopy — because in the electron microscope, you're getting all kinds of hallmarks in a cell." Auer's interests span the molecular mechanisms of hearing, breast cancer, microbial communities, and bioenergy. One area where imaging may have particular promise, he says, is in allowing researchers to see cancer stem cells in real time. "For most cancer imaging, we're looking at the wrong thing," he says. Using a combination of fluorescence imaging to mark the cells and electron microscopy to see what those cells are actually up to will be key to figuring out just how cancer cells, and stem cells in particular, differ from other cells.

Scott Fraser, director of the Beckman Institute's Biological Imaging Center at the California Institute of Technology, does a lot of live cell imaging, and he also applies a multimodal approach. Using a combination of laser scanning confocal microscopy and multiphoton imaging along with microscopic MRI, microPET, and supra-high resolution microscopy has greatly widened his scope of vision. "We like to do things so that they're multimodal, realizing that no one technique's going to be perfect," he says.



JEFF LICHTMAN

Fraser has been pushing for better labeling — one area of bioimaging that he says needs improvement. His lab is working to create

Bioimaging's Proving Grounds: Efforts to Build Brain Atlases

One area where bioimaging has seen a great deal of use is in creating high-content brain atlases. In 2006, the Allen Institute for Brain Science launched its first atlas of the mouse brain. This year, institute scientists began work on three new atlases, each of which will combine microarray with *in situ* hybridization data to create a visual map of gene expression patterns.

HANCHUAN PENG

The mouse spinal cord atlas is to be completed by the beginning of next year, and will survey all 20,000 genes of the adult and juvenile mouse spinal cord. Funding came in the form of a consortium, which developed in response to researchers' needs. Members approached the Allen Institute, according to COO Elaine Jones, and said, "'There's no normal map, we don't even know where the genes are turned on in parts of the spinal cord,' so they asked us if we would do it."

The other two projects are a map of the developing mouse brain, for which scientists will collect expression data on 3,000 genes for four prenatal and three postnatal stages; and a map of the human brain, which will look at 1,000 different anatomical structures, and then narrow that down to 50 to 500 genes of interest. "Even though that's a low number versus 20,000, if you looked at all the drugs that are manufactured, it includes less than 100 different gene targets," Jones says.

At Janelia Farm, Hanchuan Peng is working on a "comprehensive, three-dimensional, very high-resolution brain atlas," hoping to piece together image data to construct the first 3D digital map of an entire insect brain at the single-neuron level. "The ultimate goal is to try to understand how the brain works," he says. Peng is collaborating with Janelia Farm and Stanford University scientists on a 3D digital nuclei atlas for *C. elegans* and is working on construction of a high-res digital atlas of the fruitfly brain. "Once we have this structural map, we will be able to further study the function of neuronal circuits and animal behavior in a more efficient way," he says.

His lab also focuses on building new image acquisition and analysis tools. While a lot of conventional tools exist for medical imaging analysis, bioimaging is a different story. "The image has a much bigger volume," Peng says, and medical imaging tools are either too slow or "have a lot of requirements about the fine tuning of the parameters." One tool he's developed is WANO, a 3D annotation tool at the single-cell level. Peng says visualization tools also need a bit of improvement. His lab is developing a new tool called V3D, short for visualization 3D. The next step is to move toward single-cell visualization technology, he says. "The problem is, even if you can see a lot of things happening, you're not going to be able to [identify] the single cell at the whole animal level," he adds.